

**REMARKS**

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the remarks that follow.

Claims 1, 4, 14 and 15 are amended to address claim objections and indefiniteness rejections mentioned in the present action. Support for these amendments can be found throughout the specification. For example, support for the amendments to claim 1 can be found on page 15, lines 8-9 of the specification as filed. Claim 15 is amended to an independent format.

After amending the claims as set forth above, claims 1-7 and 13-15 are pending and are presented for reconsideration.

***Claim Objections***

a. The PTO objects to claim 14 for allegedly repeating the recitation of the phrase “C<sub>1</sub> to C<sub>5</sub> alkoxy” its the definition for R<sup>1</sup> in three separate instances. Applicant believes that this objection is due to the PTO’s misinterpretation of the objected phrase. According to claim 14, R<sup>1</sup> can be amongst other groups, a C<sub>1</sub> to C<sub>5</sub> alkoxy (e.g., a methoxy group), or a (C<sub>1</sub> to C<sub>5</sub>)alkoxy-(C<sub>1</sub> to C<sub>5</sub>)alkoxy group, that is, a combination of two alkoxy groups (e.g., a methoxy-methoxy group). Support for this definition for substituent R<sup>1</sup> can be found in paragraph [0029] of published application No. 2007/0149786. The above remarks should clarify the meaning of the objected phrase. Accordingly, Applicant respectfully request the PTO to withdraw the objection.

b. The PTO objects to certain terms in the definition of R<sup>4</sup> in claim 14. Specifically, the PTO objects to R<sup>4</sup> being defined as a C<sub>1</sub> alkenyl or C<sub>1</sub> alkynyl group. The present amendments to claim 14 render this objection moot.

c. The PTO states that claim 15 would be allowed if amended to an independent format. Following the PTO’s suggestion, Applicant has proceeded to rewrite claim 15 in independent form.

***35 U.S.C. § 112, second paragraph, rejections***

Claims 4 and 14 are rejected under 35 U.S.C. 112, second paragraph as being indefinite.

a. The PTO objects to the phrase “such as” in claim 4 as being unclear. The objected phrase is deleted, thus, rendering this rejection moot.

b. The PTO states that there is insufficient antecedent basis for defining substituent R<sup>3</sup> as a “C<sub>1</sub> to C<sub>10</sub> alkyl” in claim 14. Claim 14 depends from claim 1, which has been amended to provide the requisite antecedent basis for the objected term. Thus, the rejection is moot.

***35 U.S.C. § 103 rejections***

Claims 1-7 and 13-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hachisu et al. (*J. Amer. Chem. Soc.* 2003, 125, pp. 8432-8433), in view of Bachman et al. (*Journal of the American Chemical Society*, Vol. 57, No. 6, June 1935, pp. 1095-8).

The PTO admits that Hachisu neither teaches the claimed compounds or a synthetic methodology as claimed. For example, the PTO acknowledges that Hachisu teaches the synthesis of a polycyclic ketone scaffold using a base catalyzed Benzoin condensation (page 4, point (5) of the Office action), and that the disclosed polycyclic ketones would always have a hydroxyl group at the quaternary carbon atom adjacent to the keto group, which carbon is substituted with R<sup>4</sup> in the inventive compounds. Office action at page 5, point (6)

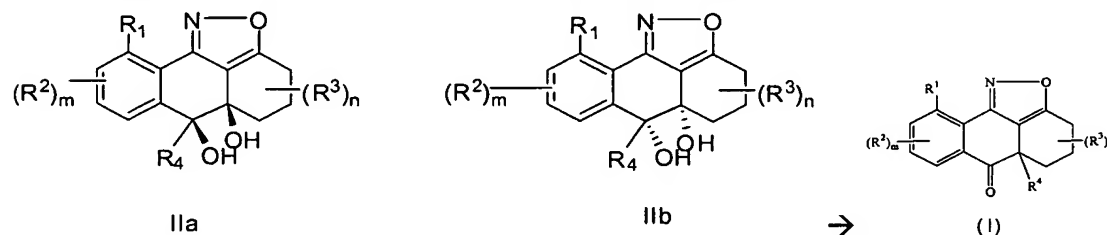
Although acknowledging these deficiencies in the teachings of Hachisu, it is the PTO's contention however, that Hachisu when combined with the teachings of Bachman would have reasonably informed a person of ordinary skill in the art a method for making Formula I compounds as claimed. The underlying rationale for such an assertion is the PTO's belief that the acid catalyzed Pinacol-Pinacolone rearrangement relied on to synthesize Formula I compounds is a well established procedure for converting diols to a ketone as evinced by a 1935 article by Bachman. Such an analysis is flawed, however, for at least the following reasons.

Bachman is focused on the synthesis and rearrangement of various 9,10-diarylhydrophenanthrenediols to the corresponding 9,9-diarylphenanthrones. To carry out this rearrangement Bachman relies on an acid catalyzed dehydration of the diol to the corresponding ketone. Bachman discloses and exemplifies the use of symmetrical diols (pinacols) for the rearrangement. That is, because the aryl groups are the same in the starting pinacols, the pinacolone product obtained is the same, irrespective of which hydroxyl group is lost during rearrangement.

A person of ordinary skill in the art would not have understood Bachman to teach or suggest the use asymmetric diols for making a polycyclic ketone as claimed, nor would a person

of ordinary skill in the art have considered Bachman's teachings pertinent to arrive at the claimed asymmetric Formula I compounds.

In sharp contrast, the inventive method is directed to the acid catalyzed rearrangement of an asymmetric diol (Formula II (a) or II(b)), to the corresponding ketone (Formula I compound).



As shown above, the net result of treating Formula II(a) or Formula II(b) compounds with an acid is loss of the quaternary hydroxyl group as water along with the migration of substituent R<sup>4</sup> to the fused quaternary carbon atom. Stated differently, the inventive method uses an asymmetric diol as the starting material to obtain an asymmetric polycyclic ketone product. As described in the specification, the inventive method has certain advantages. For example, the inventive method provides a facile route to obtaining the industrially important anthraquinone scaffold that bears a quaternary substituent, without the use of tedious multi-step protocols that employ harsh reaction conditions.

Moreover, contrary to the PTO's opinion, one of ordinary skill in the art would not have considered combining Hachisu and Bachman so as to arrive at the inventive method for synthesizing Formula I compounds. First, neither reference discloses or suggests Formula I compounds as claimed. Second, stated above, Hachisu teaches the use of a base catalyst for synthesizing the polycyclic ketone scaffold of Formula I compounds (i.e., the anthara [9,1]-isoxazole-6-one scaffold), using an intramolecular cross-aldehyde/ketone benzoin condensation reaction. Nowhere, does Hachisu teach or even suggest the acid catalyzed pinacol-pinacolone rearrangement as an alternative to the benzoin condensation, nor would the pinacol-pinacolone rearrangement have resulted in the target anthara [9,1]-isoxazole-6-one using the starting material disclosed by Hachisu.

In confirming the proper standard for determining obviousness, the Supreme Court in *KSR v. Teleflex* noted that proper inquiry should involve determining whether the improvement sought [by the claimed invention], is more than the *a priori* predictable use of known elements according to their established functions. In this vein, the Court noted that it

is "important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the [prior art] elements" in the manner claimed, that is, determine whether there was *an apparent reason to combine the known elements in the fashion claimed* by the patent at issue.

*KSR Int'l Co. v. Teleflex Inc.*, slip op. at 14 (emphasis added).

Here, neither Hachisu nor Bachman would be understood to teach or provide a motivation to alter their disclosed synthetic processes to arrive at the recited Formula I compounds, nor do these references suggest the intermediary Formula II(a) or II(b) compounds recited in claim 1. Thus, the inventive method is not obvious over the combined teachings of the cited references.

Moreover, even if it is assumed *arguendo* that the PTO's suggestion of using Bachman's pinacol-pinacolone rearrangement "to produce obvious variants of the compounds taught by Hachisu....." (Office Action at page 6), is correct, a proposition not endorsed by the Applicant, it would have been readily apparent to a person of skill in the synthetic art that such modification would change the principle of operation of the prior art invention being modified, that is, altered the chemical logic of the disclosed synthetic protocol, which as disclosed in the MPEP § 2143.01(VI), does not render the claimed invention *prima facie* obvious.

MPEP § 2143.01(VI), states that:

*"if the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims prima facie obvious."*

[Emphasis added].

The foregoing remarks provide compelling evidence in support of non-obviousness of the claimed invention. Accordingly, Applicant respectfully requests the PTO to reconsider and withdraw the section 103(a) rejection.

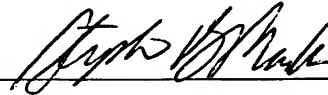
CONCLUSION

Having advanced credible remarks for the withdrawal of the outstanding issues, Applicant believes that the present application is now in condition for allowance and requests an early indication to this effect. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

Date May 7, 2010

By



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The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing or a credit card payment form being unsigned, providing incorrect information resulting in a rejected credit card transaction, or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.